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First Named Inventor	Barry J. Barclay
Art Unit	1616
Examiner Name	Dodson, Shelley A.
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Niels & Lemack		
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Serial No. : 09/900,064
Filed : July 6, 2001
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AGAINST CELLULAR DAMAGE CAUSED BY ULTRAVIOLET
LIGHT
Examiner : Dodson, Shelley A.
Art Unit : 1616
Customer No. : 42754
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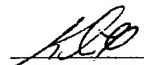
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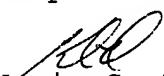
Applicant hereby claim priority of his Canadian Patent
Application No. 2,313,659 filed July 6, 2000.

A certified copy of the said Canadian Patent Application as
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Signature: Kevin S. Lemack
Date: January 9, 2006

Respectfully submitted,


Kevin S. Lemack
Attorney for Applicants
Registration No. 32,579
Niels & Lemack
176 E.Main Street-Suite 7
Westboro, MA 01581
TEL: (508) 898-818



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Specification, as originally filed, with Application for Patent Serial No: 2,313,659, on
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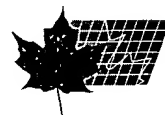
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ABSTRACT OF THE DISCLOSURE

The present invention relates generally to the use of vitamin B12 (cobalamin or cyanocobalamin) alone or in combination with other photoprotective agents, including specifically other vitamins such as vitamin B9 (folic acid or folate) and vitamin B1 (niacin or niacinamide), or any chemical derivative of these vitamins and their salts, as a filter to protect cells against the damaging effects of ultraviolet (UV) light. The invention is, in one aspect, a method of reducing the rate of UV damage to cells exposed to a UV light source, by treating the cells with the vitamin composition, either alone or in combination with other photoprotective agents. Other aspects of the invention are compositions comprising effective amounts of vitamin B12 alone or in combination with other photoprotective agents including vitamin B9 and vitamin B1 and a pharmaceutically-acceptable carrier, that are useful in protecting cells, particularly skin cells, against the burning, genotoxic (mutagenic and carcinogenic), immunosuppressive and photoaging effects of UV light, especially sunlight. The invention has application as a UV light filter in oral preparations, topical creams, lotions, sprays, wipes and cosmetics. The invention also has application as a medicinal treatment for dermatological conditions caused by exposure to sunlight, (eg actinic keratoses, photodermatitis, lupus erythematosus) and the photosensitizing effects of a variety of drugs used commonly in clinical practice (eg antihistamines, ACE inhibitors, and tetracyclines).

B COMPLEX VITAMIN COMPOSITIONS THAT PROTECT AGAINST
CELLULAR DAMAGE CAUSED BY ULTRAVIOLET LIGHT

FIELD OF THE INVENTION

The invention relates generally to sunscreens and sunfilters, and to methods and compositions for protecting cells against the damaging effects of sunlight and artificial sources of UV light such as lamps and arc welding equipment.. In particular, the invention is directed to the use of vitamin B12, alone or in combination with folate (used here to refer to the family of folic acid derivatives found commonly in nature), and niacin (specifically niacinamide) in methods and compositions for protecting cells and organisms including humans against the burning, genotoxic, immunosuppressive and photoaging effects of UV light.

BACKGROUND OF THE INVENTION

Over the past several decades, the worldwide incidence of skin cancer has been increasing at an alarming rate. The reason for this dramatic increase in skin cancers and the human suffering associated with these disorders is not entirely clear, but many experts believe that it is due, at least in part, to depletion of the earth's protective ozone layer. It is likely that the widespread use of sunscreens that protect against some but not all of the sun's harmful UV radiation (UVB but not UVA) also has played a role. According to the National

Cancer Institute (NCI), there will be over one million new cases of skin cancer reported in the United States this year. This nears the total of all other cancers combined. NCI also reported that if present trends continue 40-50% of fair skinned Americans are expected to develop at least one type of skin cancer by age sixty-five. These numbers are alarming, but in regions of the world closer to the equator, the rates of skin cancer are even higher.

In some regions of Australia for example, the probability of non-indigenous people (most of whom are of European descent) developing skin cancer at some point during their lifetime approaches 100%. Skin cancers are now the main cause of death in Australia of all persons between the ages of 25 and 40. Worldwide, skin cancer is expected to become the leading cause of death due to malignant disease in the next decade.

How did this alarming situation come about? It is likely that the worldwide pandemic of skin cancers is due to a number of causal factors. These include lifestyle choices (suntanning, increased outdoor leisure activities), an aging population (due to chronic sun exposure and decreased DNA repair capacity) dietary factors (folic acid is the most common nutritional deficiency in the world and other micro-nutrient deficiencies) and environmental factors (workplace hazards and depletion of the ozone layer). In addition to increased risk of skin cancer, exposure to sunlight has a variety of adverse effects on the human body , including erythema (burning of the skin), photoaging (wrinkling) and suppression of the immune system. Recently it has also been suggested that sunlight exposure in women might also increase the risk of neural tube defects in

the developing fetus (ref) and risk of developing endometriosis (a condition characterized by invasion of the inner lining (endometrium) tissue into the outer layers of the uterus.)

For many years it was thought by most scientific investigators that these various effects were quite separate consequences of sunlight exposure. However, recent evidence has suggested that many of the effects of solar light on the human body might be interrelated. For example, children who experience only a single episode of blistering sunburn in childhood (before the age of 18) double their risk of developing skin cancer later in life. Tanning of the skin, long thought to be an important component of a healthy lifestyle is now considered by most experts to be quite the opposite and should be more properly considered as simply the unhealthy appearance of sundamaged skin. In addition, contrary to another widely held belief, it is now well documented that tanning confers no protection whatsoever against the most serious effect of chronic sun exposure, the increased risk of skin cancer.

The skin cancers induced by sunlight can be broadly categorized into two types: melanomas and non-melanomas (basal-cell and squamous). It was generally accepted for some time that exposure to UVB (the burning rays of the sun with the wavelengths ranging from 280 to 315 nm) was responsible for the induction of melanomas, the most serious form of skin cancer and the tumor type responsible for most deaths. This was held to be especially true in those individuals who had at least one episode of severe sunburn early in childhood. It seems likely from more recent studies, (especially an elegant series of

experiments by Dr Richard Setlow reported recently to the American Academy of Dermatology that this is simply not the case. Based on spectral and mutational fingerprint analysis (each type of UV light causes a characteristic mutational pattern in target genes) Dr Setlow suggests that melanomas are due mainly to chronic exposure to UVA, wrongly considered by many people to be the harmless tanning rays of the sun, UVA has wavelengths between 320 and 400 nm. UVA has less energy than UVB but is more penetrating and passes through window glass and into deeper layers of the skin more easily.

Recent experimental evidence suggests UVB induces mainly non-melanoma skin cancers.

There are several implications of this new understanding of the carcinogenic potential of UVA and UVB. First, UVA light passes easily through the atmosphere and is not absorbed by the ozone layer. It is the main type of solar UV irradiation (about 95%) that reaches the surface of the earth. In the past, it was generally believed that UVA had only beneficial effects to humans such as stimulation of vitamin D formation and tanning. However, this is clearly not the case. Wavelengths in the UVA range induce melanomas. Second depletion of the ozone layer which permits passage of more UVB light cannot be the explanation for the dramatic increase in melanomas seen worldwide in recent years. More likely it is due to the widespread use of sunscreen products that slow burning of the skin by filtering UVB and give a false impression to the user that sundamage is not occurring. These individuals are not only at greater risk of melanoma formation but also increased risk of photoaging of the skin

suppression of their immune system. Lastly, chronic exposure to UVA over the lifetime of an individual and not acute sunburn in childhood is now considered to be responsible for the majority of melanomas, the most serious form of skin cancer and the type causing most deaths (six out of seven deaths due to skin cancer in the United States are caused by melanomas). The general implication of these findings is that tanning is unhealthy whether done in sunlight or by exposure to artificial sources of UVA such as those used in salons. It is now recommended by the US FDA that people avoid tanning salons altogether and that sunscreen products should contain both UVA and UVB filters.

The mechanism of UV damage to skin is only partly understood. The harmful effects of UVA and UVB light on human skin are due primarily to direct cellular damage (see Principles and Practice of Dermatology, 2nd Edition, Williams and Wilkins, Churchill/Livingston, N.Y.). Suppression of the immune system also occurs but by an indirect mechanism. The genotoxic potential of solar light resides mainly in the ability of UV to damage DNA (DNA absorbs maximally at 254nm). UV light causes the formation of various photoproducts in the strands of the DNA molecule. The major photoproducts caused by UV light are dimers (fusions) of adjacent pyrimidines (thymine or cytosine residues) in one of the two strands of the DNA molecule. Other minor products like 6,4 photoproducts also occur. But DNA is not the only target of UV light. UV also damages other cellular components such as collagen. This causes photoaging of the skin. But the main genotoxic (mutagenic and carcinogenic) effects of UV light seems to reside in the ability of UV wavelengths to damage DNA. The

cancer causing effects of UV light are can also reside in the ability of these wavelengths to impair the body's immunosurveillance system whose job it is to detect and destroy potentially malignant cells. In the absence of a properly functioning immunosurveillance system, skin cancers arising from cells harboring tumorigenic mutations caused by sunlight are more likely.

In the art numerous screening and filtering agents have been developed over many years, to protect skin against the deleterious affects of UV light. These agents are applied directly to the skin of a subject, and are believed to prevent UV light from penetrating the epidermis by acting as "filters," thereby absorbing or otherwise dissipating the energy contained in photons of UV light. Previously it was widely accepted in the industry that agents called "sunblocks" decreased UV-induced DNA damage, and in particular, pyrimidine dimer formation by UV opaque substances. In support of this view a recent clinical study indicated that "sunblocks" such as titanium oxide significantly reduced the incidence of pre-cancerous skin lesions in sunlight-exposed subjects. However, the term "sunblock" is no longer accepted by the US Food and Drug Agency (FDA). The FDA believes the term is misleading as no agent truly "blocks" all harmful UV rays and implies a greater degree of protection from the damaging effects of sunlight than is warranted.

Para-aminobenzoic acid (pABA), was one of the first sunfiltering agents to be identified in the art. It is now seldom used because of problems with contact dermatitis. Due to widespread use of pABA over many years about 10% of all users of sunscreen products have some degree of contact sensitivity to the

compound. However, esters of pABA, particularly octyl, dimethyl, para-aminobenzoic acid, do not elicit these same skin reactions. Other commonly used sunfilters are compounds from the salicylate, cinnamate, benzophenone, anthranilate, and dibenzoylmethane families of molecules. It is well known in the art to combine sunfiltering agents that absorb UV light in different portions of the spectrum. However, most of these agents are synthetic chemicals not found in commonly in nature and it is not known what effects longterm use of these compounds may have on the human body.

Sunscreen compositions exert their effects through filtering or absorbing UV light so that the damaging wavelengths do not penetrate the various layers of the skin. To be effective, sunscreens must be present on the skin as a continuous film, and must remain on the surface of the skin throughout the period of UV exposure. One of the problems with products currently in use is that despite numerous attempts to develop topical compositions that act as sunscreen carriers and remain on the surface of the skin (see U.S. Patent No. 5,087,445), sunscreens tend to rub off on towels and clothing, and wash off in perspiration, or during swimming, showering and bathing. Even if carriers are developed that remain on the surface of the skin for longer periods absorption of sunscreen (and cosmetic) additives into the skin remains a problem. This is due to the surprising fact that many sunfiltering agents used as sunscreen and cosmetic additives themselves cause DNA damage. Titanium dioxide for example a very common additive has long been considered to be safe and effective as a suncreening agent. This may not be the case (see Salinaro et al.,

1997, "Chemical oxidation and DNA damage catalysed by inorganic sunscreen ingredients" FEBS Lett **418**:87-90). Padimate-O, another common sunscreen additive in widespread use may also be genotoxic (see P.J. McHugh and J. Knowland, 1997, "Characterization of DNA damage inflicted by free radicals from a mutagenic sunscreen ingredient and its location using an in vitro genetic reversion assay" Photochem Photobiol **66**:276-281.]

A recent research article (G.J. Cameron et al., 1997, "Systemic absorption of sunscreen after topical application" The Lancet **350**: 863-864) has shown that the UVA sunscreen oxybenzone, a benzophenone derivative used commonly worldwide to make sunscreen products with high sun protection factors (SPF) is absorbed systemically and excreted in human urine soon after application to the skin. The repeated use of a sunscreen that is absorbed systemically could pose an especially high risk to human health if the sunscreen agent is chronically genotoxic. A recent and alarming finding is that at low concentration most if not all of the sunscreen agents currently in use are both mutagenic and tumorigenic (R C von Borstel, personal communication). The tumor incidence was very high in along the borders of applied sunscreen in experimental animals.

These findings have added a new urgency to the development of novel sunfiltering agents that are not only effective in reducing the harmful effects of UV light, but are also safe, even upon repeated usage and over a long period of time. Subsequent to experiments on the role of the vitamin folic acid in the repair of UV damage to DNA (see Barclay et al exp med boil 1993) my collaborators and I discovered what we believe might be a natural sunfilter in the human body.

The compound is a folate which occurs naturally in the bloodstream and is also associated with hemoglobin in red blood cells.

SUMMARY OF THE INVENTION

The object of the invention is to provide a means of reducing the burning, genotoxic, immunosuppressive and photoaging effects of UV light by application of three common B vitamins to the skin

The term "vitamin B12", "folate" and "niacinamide" as used herein, includes the parent compounds, their precursors (pro-vitamins), metabolites, derivatives, and their conjugates, all of which may be either naturally occurring or synthetic, as well as the salts of the compounds. Results of experiments with human volunteers described below have shown that the combination folic acid, vitamin B12 and niacinamide when taken in pill form prevented sunburning for many hours. It is assumed that topical application would be effective in a similar fashion.

Broadly speaking, the invention provides a method for reducing UV damage to cells, comprising exposing the cells to an amount of at least one of vitamin B12 or folate but preferably the two vitamins in combination with niacinamide, in appropriate concentration, which is sufficient to reduce UV damage to cells, specifically skin cells. In one embodiment, the invention is a method for reducing UV damage to the outer cell layers of a subject, comprising administering to the subject a formulation of vitamin B12, folate and niacinamide, in a suitable carrier, the amounts of each individual component sufficient to

reduce UV damage to cells. In one preferred embodiment, the carrier is suitable for topical application, and the composition is applied to the skin of the subject. In another preferred embodiment, the carrier is suitable for oral administration, and the composition is ingested by the subject. In another preferred embodiment, the three B vitamins, in suitable carriers, are administered to the subject both topically and orally, in combination. In an particularly preferred embodiments, the folate is leucovorin, folic acid, or a combination of these two folates.

Broadly speaking, the invention also provides compositions for reducing UV damage to cells, comprising vitamin B12, niacinamide and at least one folate, and a suitable carrier. In one preferred embodiment, folate is present in the composition at a concentration in the range of approximately 0.1 to 3mg/ml and, the carrier is suitable for topical application. Niacinamide is present at approximately 100X this amount ie 1.0 to 30mg/ml. Vitamin B12 is present in the range 0.1 mg to limits of its solubility. In another preferred embodiment, a folate is present in the composition in a total dosage of up to 10.0 mg, niacinamide in an amount up to 1000 mg, vitamin B12 up to 1.5 mg and the carrier is suitable for oral administration. In a particularly preferred embodiment, the folate is leucovorin, folic acid, or a combination of these two folates or their pharmaceutically-acceptable salts.

The claimed invention has the advantage that administration of the vitamin mixture containing vitamin B12, a folate, and niacinamide, for the purposes of reducing UV damage to the cells of a subject can be done either

topically, systemically (orally or by injection), or via a combination of routes. Systemic delivery of the vitamin mixture might afford protection to the eye, something that cannot readily be accomplished by commercially available topical sunscreens. Such a treatment might be expected to lessen the risk of cataracts induced by UV light. Secondly, protection from UV light by a naturally occurring compound may avoid exposure to chemicals that may be toxic, genotoxic (mutagenic or carcinogenic) or irritating to the subject. Thirdly, the invention provides a method to filter or absorb harmful UV rays through the use of bioavailable compounds. Bioavailable compounds are chemicals, usually from natural sources, that are readily taken up and metabolized by cells. Because these compounds are simple B complex vitamins with other known effects their ingestion or topical application may have other health benefits than those described herein. Other features and advantages of the invention will be evident from the following description and the claims.

DETAILED DESCRIPTION OF THE INVENTION

Vitamin B12

Folates

A number of folates, described below, are applicable to the invention. For the purposes of this patent application, the term "folate" or "folates" mean folic acid, its precursors, its metabolites, its derivatives, including polyglutamated derivatives, its conjugates, as well as the salts of the foregoing compounds, all of

which may be naturally occurring or synthetic. "Reduced folates" means folates at the dihydro and tetrahydro level of oxidation, for example folinic acid or folinate. The folates referred to above include, but are not limited to, the following: folic acid, dihydrofolic acid, tetrahydrofolic acid, 5-formyltetrahydrofolic acid (folinic acid, leucovorin), 10-formyltetrahydrofolic acid, 5-10 methylenetetrahydrofolic acid, 5-10 methenyltetrahydrofolic acid and 5-methyltetrahydrofolic acid. Of these, folic acid and folinic acid and their salts are preferred.

Folic acid is formed from three separate chemical building blocks:

- a heterocyclic pteridine ring, 6-methylpterin
- p-aminobenzoic acid (pABA), and
- glutamic acid.

The 6-methylpterin moiety is linked through the amino group on pABA to form pteric acid, which is in turn linked through an amide to glutamate. Pteric acid that is linked to a single glutamate is known as pteroylmonoglutamate. However, many naturally occurring folates have additional glutamate residues attached to pteric acid (pterylpolyglutamates). The additional glutamate residues, linked by means of a modified peptide bond involving the alpha-amino group of one glutamate and the gamma-carboxyl group of another, allow for compartmentalization of different reduced folates in cells and provide an additional level of regulation for folate interconversion enzymes.

It is believed that only the monoglutamate forms of folate are transported into human cells. Other glutamate groups are added subsequently. One function

of these polyglutamated derivatives is to maintain intracellular pools of reduced folates. The term folate, as used herein includes such polyglutamated derivatives.

Humans cannot synthesize folic acid de novo. Inside cells, folic acid is metabolized to dihydrofolate and then to tetrahydrofolate by means of an enzyme known as dihydrofolate reductase (DHFR). Tetrahydrofolate is converted to a variety of reduced intermediates involved in the mobilization and utilization of single-carbon functional groups (i.e. methyl, methenyl, methylene and formyl). These one carbon donors function in the metabolism of certain amino acids such as serine, glycine, methionine, and histidine, and in the biosynthesis of purine and pyrimidine nucleotides. In the latter pathway a reduced folate donates the methyl group of thymine via thymidylate synthase without which cells lack one of the basic building blocks of DNA synthesis. Consequently, depletion of reduced folates (usually due to DHFR inhibition) is lethal to cells. The effects of partial folate starvation on cells is not known but it is reasonable to suppose that they are impaired in nucleotide synthesis and thus cannot synthesize and repair DNA at normal rates.

Pathways for the biosynthesis, interconversion, and utilization of a number of naturally occurring folates in human cells are illustrated in Figure 1.

Many folates exist in nature, but they can also be manufactured by chemical synthesis. For purposes of this application, the term folate encompasses both naturally occurring and synthetic forms.

Folates can be used as a single chemical species or a mixture of two or more species. It is anticipated that a mixture of folates may be more effective than a single species. For example, the UV absorption spectra of folic acid and folinic acid cover a broader spectrum of absorption than either compound alone.

Some of the folates of the invention can be obtained commercially from a number of sources. Folic acid, folinic acid and 5-methyltetrahydrofolate acid are available from Sigma Chemical Co., St Louis Mo. Other folates that are not commercially available can be prepared by a chemist of ordinary skill in the art, (see U.S. patent no. 5,410,056, which is hereby incorporated by reference in its entirety)

Conjugates of the folates such as those with amino acid side chains can be prepared by published methods (see Ayling, J. and Baugh, N., Chemistry and Biology of Pteridines and Folates, 1993, Plenum Press NY, which is hereby incorporated by reference in its entirety).

The folates of the invention need not be highly purified. Mixtures of partially purified folates can be used. Folates or combinations of folates can be tested for their ability to protect cells from UV light, by using the a screen such as the human fibroblast cell culture system described herein. The folates to be tested would be added to cultures of mammalian cells before, during or after exposure to UV light. Folates that are effective blocks to UV light would increase cell survival.

Administration of the B Vitamin Formulation

The methods of the invention are applicable to cells of any organism that can potentially be damaged by UV light. For the purposes of this patent application, the term "subject" means a whole multi-cellular organism, which includes humans, lower animals and plants. In a preferred embodiment, the methods and compositions are applied to human cells, particularly human cells which are subject to sun exposure, such as melanocytes, and the squamous and basal cells of the dermis and epidermis.

For cells that are maintained in tissue culture, the vitamins are administered by adding them to the growth medium in which the cells are maintained.

For whole organisms, including humans, the compounds may be administered topically, by applying them to the outside skin or surface of the organism. Without being bound by any theory, it is suggested that the folates used in the invention act both extracellularly and intracellularly. Many types of cells are permeable to at least some of the folates that are used to carry out the invention. For example, mouse L1210 cells, can take up folates such as 5-methyltetrahydrofolate, by at least two mechanisms; a specific transporter in the cell membrane that operates in the micromolar range and a second transport system that takes up folates in the nanomolar range.

A lack of permeability to a particular folate does not necessarily exclude the compound from intracellular use. Various methods can be used to facilitate the entry of the folates into cells. For example, the liposome-mediated methods, which have been developed for the delivery of DNA repair enzymes, as

mentioned above, can be adapted to deliver the three B complex vitamins into cells. Such methods are disclosed in US Patent Numbers 5,077,211 and 5,352,458, which are hereby incorporated by reference in their entirety.

For purposes of administration of the three B vitamins alone or in combination to a subject, they are incorporated into a pharmaceutically acceptable carrier, which can take many different forms. By "pharmaceutically-acceptable" is meant that the carrier comprises common pharmaceutical and cosmetic ingredients that are generally recognized as safe for human use. A suitable topical carrier can be in the form of a water-in-oil emulsion. These emulsions can be thin or thick in consistency, so as to be adaptable to spray or aerosol delivery, lotions, creams, etc. Some folates are water-soluble, and can be used without an oil component in the carrier.

If it is desired to deliver the three B vitamins into cells, oral or paranteral routes can be used.

Methods and compositions for administration via oral and parenteral routes are well known in the art. (For example, see Ansel, A. C., Popovich, N.G., and Allen Jr., L.V. Pharmaceutical Dosage Forms and Drug Delivery Systems, 6th Edition. 1995. Williams & Wilkins, Baltimore, which is hereby incorporated by reference in its entirety.) Topical application to the epidermis of a subject can also be an effective route to deliver bioavailable folates, niacinamide and vitamin B12.

Many appropriate carriers for topical administration are described in the above-noted reference by Ansel et al., including ointments, creams, sprays and

lotions. Other appropriate carriers are disclosed in the following patents, hereby incorporated by reference: US 4,401,664, US 4,938,969, US 5,607,622, and US 5,153,230.

The B complex vitamin formulation could also be administered via micro sponge delivery system, as described in K. Embil and S. Nacht, 1996, "The micro sponge Delivery System (MDS): a topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives" J Microencapsul 13: 575-588.

Although topical or oral delivery would seem the most practical, for some human subjects who are extremely light sensitive due to treatment with various prescription medicines(eg tetracycline) or who are afflicted with certain medical conditions (eg burn patients) or genetic disorders (eg xeroderma pigmentosum), it is conceivably advantageous to deliver the composition systemically by means of intravenous, subcutaneous or intra-muscular routes.

The compositions used in the invention may contain additional ingredients in addition to folates and suitable carriers. The compositions may also contain various agents whose purpose is mainly cosmetic or esthetic, such as perfuming agents, colorants, etc. The composition may also contain other compounds used as sunblocks, or to prevent photoaging of human skin. These include but are not restricted to: cinnamate, benzophenone, beta-carotene, and alpha-hydroxy acids. In particular, Vitamin E (alpha-tocopherol), often used in commercial skin care products could be incorporated into the composition.

The composition may also contain agents that promote absorption into the skin, for example, propylene glycol, which was used in Example 1 and 2. The folate compounds of the invention could also be administered in liposomes, or liposomes that also contain DNA repair enzymes, as outlined in US Patent Numbers 5,077,211 and 5,352,458.

The appropriate concentration of folates in the composition to be administered to a subject varies depending on the particular folate, the route of administration, and the cells to which it is targeted. However, for intracellular effects, the concentration of folates should be tailored to result in the accumulation in the cells of sufficient concentrations of the three B complex vitamins to reduce UVR damage to the cells. For UV absorption or blocking on the outer surfaces of the subject, the concentration of vitamins should be adjusted to result in the desired degree of absorption or blocking. Preferably, the concentration of folates in the composition is between (0.002 and 10 mg/ml), and more preferably between (0.002 mg/ml and the limits of solubility of the folate compound in any particular carrier). The concentration of niacinamide will be 100 times this amount. The vitamin B12 concentration will be in the range 0.1 mg/ml to the limits of solubility of the vitamin. The topical composition can be reapplied periodically during sun exposure to replace removed or absorbed material.

If the three B complex vitamins are administered orally, the composition, in a suitable carrier, can be administered daily or several times during the day. The composition could be administered in a pill or capsule, orally or sub-lingually

or in the form of a juice or other suitable drink. A daily dosage of folates in the range of 0.02 mg/kg to 0.05mg/kg, and preferably between 0.02 mg/kg and 0.2 mg/kg, and more preferably between 0.02mg/kg and 1mg/kg can be ingested orally. The amount of niacinamide will be 100 times this amount. Vitamin B12 can be ingested in the range 0.001 mg/kg to 1 mg/kg.

The effective amount of a particular B complex vitamin can readily be determined by a person skilled in the art by a variety of common assay systems.

Drawings: none

Experimental Evidence:

Claims:

I claim:

1. A method for reducing the damaging effects of ultraviolet radiation to cells of a subject comprising exposing the cells to an effective amount of a composition containing vitamin B12.
2. The method of Claim 1 wherein the composition is taken orally
3. The method of Claim 1 wherein the composition is applied to the skin.
4. The method of Claim 1 wherein the composition is taken by injection.
5. The method of Claim 1 wherein the composition in addition to vitamin B12 also comprises at least one anti-photoaging compound.
6. The method of Claim 1 wherein the composition comprises in addition to vitamin B12 at least one sunfiltering or suncreening compound including other vitamins.
7. The method of Claim 1, wherein the subject is an animal.
8. The method of Claim 1 wherein the animal is a human.
9. The method of Claim 1 wherein the composition is incorporated into a liposome.
10. The method of Claim 1 wherein the composition also comprises at least one DNA repair enzyme.
11. The method of Claim 2 wherein the amount of vitamin B12 ingested is between 0.1 mg and 1.5 mg.
12. The method of Claim 2 wherein the composition also contains any folate in the range 1 mg to 10 mg.

13. The method of Claim 2 wherein the composition also contains niacin or any derivative of niacin in the range 100 mg to 1 g.
14. The method of Claim 1 wherein the composition is applied to the to the skin of the subject in a continuous film.
15. The method of Claim 14 wherein the composition comprises vitamin B12 at a concentration of between 0.1 mg/ml and 10 mg/ml in a pharmaceutically-acceptable carrier.
16. The method of claim 14 wherein the composition comprises in addition to vitamin B12 any folate at a concentration of between 0.2 mg/ml and the upper limit of solubility of the compound in a pharmaceutically-acceptable carrier.
17. The method of claim 14 wherein the composition comprises in addition to vitamin B12, niacinamide or any derivative of niacin in the concentration range 2 mg/ml and the upper limit of solubility of the compound, in a pharmaceutically acceptable carrier.
18. The method of Claim 4 wherein the composition comprises vitamin B12 in an amount between 0.1 mg and 1.5 mg.
19. The method of Claim 4 wherein the composition contains, in addition to vitamin B12, any folate in the range 1 mg to 10 mg.
20. The method of Claim 4 wherein the composition contains, in addition to vitamin B12, niacinamide or any derivative of niacin, in the range 100 mg to 1 g.

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